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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,433	03/05/2002	Caroline Connelly	09100.020	3339

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KAREN LEE ORZECOWSKI
IP LAW SPECIALISTS, llc
7777 LEESBURG PIKE
SUITE 304 NORTH
FALLS CHURCH, VA 22043

EXAMINER

GITOMER, RALPH J

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/857,433

Applicant(s)

CONNELLY ET AL.

Examiner

Ralph Gitomer

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15, 18, 19 and 21-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15, 18, 19 and 21-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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Applicant's election without traverse of Group I, claims 1-15, 18, 19, 21-23 in the reply filed on 9/27/04 is acknowledged. A flow chart or diagram of the features shown beginning on page 15 of the present specification would assist in understanding the claimed invention. The specification lacks standard headings and organization, for example there is no Brief Description of the Drawings. The abstract contains legal terminology. Please also update the specification regarding related cases and priority.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 5, 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coombs.

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Claim 1 may differ from Coombs in that it recites the reducing agent is acted upon or inactivated after the enzyme reacts with the sample. Claim 3 recites a stabilizer for the reaction mixture. Claim 5 recites the sample is removed from the assay.

Coombs (6,306,618 B1) entitled "Homocysteine Desulphurase from the Protozoan *Trichomonas Vaginalis*" teaches in column 7, treating a sample to determine total homocysteine with a reducing agent to cleave any disulfide bonds and liberate free homocysteine. The resulting ketobutyrate is detected by adding NADH and lactate dehydrogenase to generate NAD⁺ which is determined. In column 9 line 6 DTT is a reducing agent. In column 18 Assay II, dithiothreitol is added, then homocysteine desulphurase, then lactate dehydrogenase to release NAD⁺, pH is changed and NAD is fed into a cycling reaction to generate a colored product. See the claims.

It would have been obvious to one of ordinary skill in this art at the time the invention was made to inactivate the reducing agent because Coombs teaches in Assay II, step 2, a dye is added in an HCl solution which would to some degree inactivate the DTT reducing agent. Regarding the stabilizer of claim 3, it is well known in this art and taught by a number of the references cited herein that stabilizers are commonly added to enzymes of many types to store them and maintain their activity. No enzyme activity is claimed. Regarding claim 5 which recites removing the sample, the homocysteine of the sample would be removed by enzymatic activity and no longer be present after reacting with the desulphurase.

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Claims 4, 6, 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tan.

Tan (5,998,191) entitled "High Specificity Homocysteine Assays for Biological Samples" teaches in column 16, centrifuging the sample, adding DTT, and adding homocysteinase. Hydrogen sulfide is measured. In column 18 Example 6, pyruvate is detected independently of hydrogen sulfide. In column 19 lactate dehydrogenase is added to react with the pyruvate. In column 19 lines 41-45, protein free filtrates of samples are shown.

Claim 4 differs from Tan in that the claims are directed to pyruvates that are deactivated prior to the homocysteine enzyme is reacted where Tan teaches assaying pyruvates separately from homocysteine. Claims 6 and 18 differ from Tan in that the sample is both filtered and centrifuged to remove pyruvates.

It would have been obvious to one of ordinary skill in this art at the time the invention was made to assay homocysteine specifically and to not include interfering pyruvates by eliminating the pyruvates or assaying them separately as a correction factor to determine the homocysteine. The result would be the same to perform a homocysteine assay either way. And Tan teaches filtering the sample to remove proteins and to both filter and centrifuge to remove proteins would have the expected result. Both filtering and centrifuging to remove desired components is well known in this art.

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Claims 7, 8, 9, 11, 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of Coombs and Tan or the combination of Coombs in view of Tan.

Claims 7-9, 11 differ from the above references in that they employ more than one assay to determine homocysteine where each reference teaches there are a number of different assays but show only a single assay for the determinations.

It would have been obvious to one of ordinary skill in this art at the time the invention was made to employ any number of known assays for their known function with the expected result. No novelty is seen in selecting any of the known assays in any desired combination. No specific advantage is seen in doing so and an undisclosed advantage is given little or no weight. No results of such a combination of assays is claimed.

The cycling NAD⁺/NADH reaction of dependent claims 21-23 is taught by Coombs for the same function as presently claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15, 18, 19, 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of the following applies in all occurrences.

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The claims must be carefully rewritten in accordance with standard US Patent practice. Method claims commonly recite the steps of contacting, determining, correlating. In claim 1, "characterized in that" may be intended to be wherein. In claim 1 "depotentiates" is queried as it is not a term of art. In claim 2, "lyphilisate" is queried as it is not a term of art. All independent claims must begin with an indefinite article and dependent claims begin with a definite article. In claim 4 "homocysteine converting enzyme" is unclear as to what may be intended. Is the enzyme converted by the homocysteine? What is converted to what is not seen. In claim 5 last line, "removed from the assay" is unclear as to what is removed from what. As stated the assay would not work because if the sample were removed, there would be no homocysteine present. In claim 6, "exclusion filter" does not state what is excluded from what. In claim 14 "ate" is a typo. In claim 19 "HDS" should be spelled out in the first occurrence in the claims. In claim 22 "the initial biological fluid sample" lacks antecedent basis.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Rozzell (5,885,767) teaches homocysteine assays.

Xu (6,066,467) teaches homocysteine assays.

Kawasaki (6,635,438) teaches homocysteine assays.

Matsuyama (6,686,172) teaches homocysteine assays.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ralph Gitomer whose telephone number is (571) 272-0916. The examiner can normally be reached on Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Ralph Gitomer
Primary Examiner
Art Unit 1651

RALPH GITOMER
PRIMARY EXAMINER
GROUP 1200